Long-term outcomes of standard endovascular aneurysm repair in patients with severe neck angulation

Nelson F. G. Oliveira, MD,[a,b] Frederico Bastos Gonçalves, MD, PhD,[a,c] Sanne E. Hoeks, PhD,[d] Marie Josee van Rijn, MD, PhD,[a] Klaas Ultee, PhD,[a] José Pedro Pinto, MD,[a,e] Sander Ten Raa, MD, PhD,[a] Joost A. van Herwaarden, MD, PhD,[f] Jean-Paul P. M. de Vries, MD, PhD,[g] *and* Hence J. M. Verhagen, MD, PhD,[a] *Rotterdam, Utrecht, and Nieuwegein, The Netherlands; and Azores, Lisbon, and Porto, Portugal*

ABSTRACT

Objective: Severe neck angulation is associated with complications after endovascular aneurysm repair (EVAR). Newer endografts may overcome this limitation, but the literature lacks long-term results. We studied the long-term outcomes of EVAR in patients with severe neck angulation.

Methods: A retrospective case-control study of a prospective multicenter database was performed. All measurements were made with dedicated software with center lumen line reconstruction. A study group including patients with neck length >15 mm, infrarenal angle (β) >75 degrees or suprarenal angle (α) >60 degrees, and neck length 10 to 15 mm with β >60 degrees or α >45 degrees was compared with a control group matched for demographics and other morphologic neck features. The primary end point was type IA endoleak (EL1A). Secondary end points were freedom from neck-related secondary interventions, primary clinical success, and overall survival.

Results: Forty-five patients were included in the angulated neck group and compared with 65 matched patients. Median follow-up was 7.4 years (interquartile range, 4.8-8.5 years). In the angulated neck group, mean α was 51.4 degrees (±21.1 degrees) and the mean β was 80.8 degrees (±15.6 degrees); in the nonangulated group, these were 17.9 degrees (±17.0 degrees) and 35.4 degrees (±20.0 degrees), respectively. At 7 years, five patients in the angulated neck group and two nonangulated patients developed EL1A, yielding a freedom from EL1A of 86.1% (n = 14; standard error [SE], 0.069) and 96.6% (n = 34; SE, 0.023), respectively (P = .056). After exclusion of a patient who developed an EL1A secondary to an endograft infection, this difference was significant: 86.1% (n = 14; SE, 0.069) in the angulated neck group and 98.2% (n = 34; SE, 0.018) in the nonangulated group (P = .016). At 7 years, freedom from neck-related secondary interventions was 91.7% (n = 14; SE, 0.059) and 91.6% (n = 29; SE, 0.029), respectively. The 7-year primary clinical success estimates were 41.2% (n = 11; SE, 0.085) and 56.6% (n = 20; SE, 0.072) for the angulated neck and nonangulated groups, respectively (P = .12). The 7-year survival rates were 44.3% (n = 18; SE, 0.076) vs 66.7% (n = 42; SE, 0.059) for the angulated neck and nonangulated groups, respectively (P = .25). Device integrity failure was not observed.

Conclusions: Despite satisfactory results early and in the midterm, a higher rate of EL1A was identified among patients with severely angulated necks in the long term. However, mortality was not affected by this difference. These findings suggest that EVAR should be used judiciously in patients with extreme angulation of the proximal neck and highlight the need for close follow-up of EVAR, especially in the long term and in patients treated outside instructions for use. (J Vasc Surg 2018;68:1725-35.)

Keywords: Aortic aneurysm; Abdominal; Blood vessel prosthesis implantation; Severe aortic neck angulation; Long-term follow-up; Endurant stent graft; Retrospective studies

Endovascular aneurysm repair (EVAR) has become the preferred treatment for infrarenal abdominal aortic aneurysms (AAAs).[1] Long-term outcome after EVAR depends greatly on achieving durable seal. Severe neck angulation has been associated with loss of seal, type IA endoleak (EL1A), endograft migration, and aneurysm sac enlargement after EVAR.[2-4] Consequently, many endograft manufacturers have limited this risk by defining angulation thresholds in each endograft's instructions for use (IFU) that reflect the

From the Department of Vascular Surgery[a] and Department of Anesthesiology,[d] Erasmus University Medical Center, Rotterdam; the Department of Angiology and Vascular Surgery, Hospital do Divino Espírito Santo, Ponta Delgada, Azores[b]; the Department of Angiology and Vascular Surgery, Hospital de Santa Marta, Centro Hospitalar de Lisboa Central, Lisbon[c]; the Department of Angiology and Vascular Surgery, Hospital de São João, Porto[e]; the Department of Vascular Surgery, University Medical Center Utrecht, Utrecht[f]; and the Department of Vascular Surgery, St. Antonius Hospital, Nieuwegein.[g]

Author conflict of interest: N.F.G.O. has received an educational research grant from the Lijf en Leven Foundation. F.B.G. receives consulting and proctoring fees from Medtronic and W. L. Gore. S.E.H. has received an educational research grant from the Lijf en Leven Foundation. J.A.H. is a consultant for Medtronic and Bolton Medical. J.M.P.M.V. is a consultant for Medtronic. H.J.M.V. is a consultant for Medtronic, W. L. Gore, Endologix Arsenal AAA, and Philips.

Correspondence: Nelson F. G. Oliveira, MD, Erasmus University Medical Center, 's-Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands (e-mail: n.gomesoliveira@erasmusmc.nl; nfgoliveira@sapo.pt).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2018.03.427

expected performance of each endograft in such anatomies.

The Endurant stent graft (Medtronic, Santa Rosa, Calif) is specifically engineered to adapt to challenging neck anatomy.[5,6] Features such as its increased conformability and active fixation have yielded good results at midterm in severely angulated neck anatomy, but long-term data are lacking.[7]

This study investigates the impact of severe proximal neck angulation on long-term outcomes after EVAR with the Endurant stent graft system.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of a prospectively collected multicenter database
- **Take Home Message:** Endovascular aneurysm repair in 45 patients with angulated necks and in 65 controls resulted in similar rates of neck-related reinterventions and survival after 7 years but higher rates of type I endoleaks in the angulated neck group.
- **Recommendation:** This study suggests that standard endovascular aneurysm repair leads to higher rates of type I endoleaks in aneurysms with angulated necks after long-term follow-up.

METHODS

Population of patients. This is a case-control study including a group of 110 patients treated with the Endurant stent graft. Study methodology and short-term and midterm outcomes have been reported previously for this same cohort.[8,9] Briefly, this study was based on a prospective database from three high-volume centers in the Netherlands (Erasmus University Medical Center, Rotterdam; St. Antonius Hospital, Nieuwegein; and University Medical Center, Utrecht). During the study period (2008-2009), treatment selection was individualized according to anatomic determinants, health status, history of previous abdominal surgery (hostile abdomen), and preference of the patient. During the study period, 418 patients underwent EVAR in these centers, including elective implantation of 271 primary Endurant stent grafts for degenerative AAA. Patients with mycotic aneurysms or prior abdominal aortic interventions were excluded. All patients with severe proximal neck angulation treated outside the endograft's IFU were identified.[10] Specifically, patients were included in the study group if they presented with one of the following combinations: neck length >15 mm with an infrarenal angle (β) >75 degrees or suprarenal angle (α) >60 degrees; or neck length 10 to 15 mm with β >60 degrees or α >45 degrees. Inclusion was due to β angle exclusively in 23 patients (51.1% of the angulated group) and α angle in 8 (17.8%); in 14 (31.1%), both α and β angulation were within the inclusion criteria. During the study period, all EVAR patients with angulated necks were treated consecutively with Endurant stent grafts. A control group of 65 patients treated with the same device and matched for demographics and baseline clinical characteristics was selected from the remaining elective standard EVAR population from the same hospitals and time period. Demographic and anatomic data were acquired at the time of surgery. All subsequent follow-up data were prospectively obtained on review of the patient's electronic file. This study complies with the Declaration of Helsinki in research ethics. Informed consent was waived according to institutional policy on retrospective research studies.

Postoperative surveillance. At the beginning of the study period, postoperative follow-up included computed tomography angiography (CTA) at 1 month, 12 months, and yearly thereafter. Since then, and according to the treating physician's judgment, in the majority of the patients, yearly CTA imaging has been replaced by color duplex ultrasound (DUS) or non-contrast-enhanced computed tomography (CT), particularly in patients with expected lower risk of complications or renal function impairment. If endoleak or aneurysm growth was detected, patients would then undergo CTA imaging.

Image analysis and measurements. All anatomic measurements (angulation, diameters, length, and volume) were obtained from semiautomatically generated center lumen line (CLL) orthogonally reconstructed imaging, performed on a workstation with dedicated software (3mensio Vascular 4.2; Pie Medical, Bilthoven, The Netherlands). All imaging data were obtained by two observers with extensive experience in image analysis (N.F.G.O., F.B.G.). In previous reports, our group has demonstrated high rates of interobserver agreement regarding aneurysm and neck diameter, neck length, proximal seal length, and aneurysm volume measurements obtained with this methodology.[11,12] Angulation determination has been reported previously and was performed according to a standardized and validated method.[13] In summary, using the same CLL reconstruction, the aorta is rotated along its CLL axis until the sharpest angle is found. The α angle was measured between the suprarenal aorta and infrarenal neck and the β angle between the infrarenal neck and aneurysm sac. As previously reported, good agreement between the two observers responsible for the acquired measurements used in this study was obtained for both suprarenal and infrarenal angle measurements.[9]

Definitions. Patients' demographics and outcomes are presented according to the Society for Vascular Surgery/American Association of Vascular Surgery Ad

Table I. Baseline clinical, anatomic, and device-related characteristics

Characteristic	Angulated (n = 45)	Nonangulated (n = 65)	*P* value
Age, years	75.6 (±6.5)	72.7 (±8.5)	.49
Male sex	36 (80.0)	59 (90.8)	.11
Smoking	32 (71.1)	51 (78.5)	.38
Hypertension	25 (55.6)	35 (53.8)	.70
Cardiac disease	22 (48.9)	27 (41.5)	.45
Diabetes	6 (13.3)	15 (23.1)	.20
COPD	14 (31.1)	13 (20.0)	.18
Creatinine clearance <60 mL/min/1.73 m^2	16 (35.6)	20 (30.8)	.60
Cerebrovascular disease	4 (8.9)	12 (18.5)	.16
Peripheral arterial disease	11 (24.4)	15 (23.1)	.87
ASA class 3/4	33 (73.3)	43 (66.2)	.42
AAA diameter, mm	68.6 (14.2)	58.8 (7.6)	<.001
AAA volume, mL	309.5 (30.1)	187.4 (8.2)	<.001
Proximal neck diameter, mm	25.2 (4.2)	25.5 (4.5)	.71
Proximal neck length, mm	27.2 (14.8)	32.6 (13.1)	.05
Neck thrombus >25% of circumference	8 (17.8)	10 (15.4)	.74
Neck calcification >25% of circumference	3 (6.7)	1 (1.5)	.16
α Angle, degrees	51.4 (21.1)	17.9 (17.0)	<.001
β Angle, degrees	80.8 (15.6)	35.4 (20.0)	<.001
Oversizing, %	21.4 (±10.2)	16.1 (±9.4)	.01
Proximal seal length on 30-day imaging, mm	16.6 (±8.1)	20.9 (±8.5)	.02
Follow-up time, years	5.7 (2.6-8.3)	7.8 (5.9-8.6)	.02

AAA, Abdominal aortic aneurysm; *ASA,* American Society of Anesthesiologists classification; *COPD,* chronic obstructive pulmonary disease.
Continuous data are presented as mean (±standard deviation) or median (interquartile range [IQR]) and dichotomous data as number (%). Neck thrombus and neck calcification are presented as >25% of circumferential involvement by each of the features within the proximal seal zone.

Hoc Committee for Standardized Reporting Practices in Vascular Surgery guidelines.[14] AAA-related adverse events were defined by any of the following: type I, type III, or undetermined endoleaks; postimplantation sac growth; migration >10 mm; device integrity failure; AAA-related death; AAA rupture; or any AAA-related secondary intervention. Secondary interventions were considered neck related if they were performed to resolve or to prevent a possible complication related to the proximal seal zone (including implantation of Palmaz stent, proximal standard or fenestrated cuff insertion, aortouniiliac conversion, or open conversion due to loss of proximal seal with or without an associated endoleak). Primary clinical success was defined by the absence of any AAA-related adverse event during follow-up.

Neck diameters were determined in two perpendicular axes just below the lowermost renal artery and at every 5 mm along the infrarenal neck on CLL imaging for 15 mm. The reference neck diameter was the average of the two largest outer-to-outer neck measurements. In patients with a neck length <15 mm, the average of the first two measurements was taken as the reference diameter. Oversizing was calculated by dividing the difference between the implanted endograft diameter and the reference neck diameter by the latter. Proximal seal length was measured on the CLL reconstructed image as the length of total circumferential apposition of the endograft to the aortic wall, as previously reported.[11] For proximal seal determination and barb detachment, center lumen markers were manually placed from at least the origin of the superior mesenteric artery to the endograft's flow divider for every 2 mm. Likewise, endograft to renal artery distance was measured between the lowermost renal artery and the first covered stent. Migration was calculated in subsequent imaging by subtracting the 30-day endograft to renal artery distance from the same distance measured on the latest postoperative CT. Barb detachment was defined as nonapposition of a suprarenal stent barb to the aortic wall. Neck configuration was classified according to previously reported nomenclature.[15] Accordingly, neck diameter variations of 10% were considered indicative of nonparallel aortic walls. Aortic necks demonstrating progressive diameter increments ≥10% were considered inverse-tapered necks.

End points. The primary end point was EL1A. Freedom from proximal neck-related interventions, primary clinical success, and overall survival were also assessed. Finally, the evolution of infrarenal neck morphology was also analyzed, as were endograft-related outcomes in the aortic neck.

Table II. Long-term outcomes after endovascular aneurysm repair (EVAR)

	Univariable		
	Angulated (n = 44)	Nonangulated (n = 63)	*P* value
Primary clinical success	30 (68.2)	41 (65.1)	.122
Secondary clinical success	39 (88.6)	50 (79.4)	.010
All-cause mortality	25 (56.8)	35 (55.6)	.252
Late aneurysm-related mortality	2 (4.6)	1 (1.6)	.276
AAA-related adverse events	9 (20.5)	17 (27.0)	.995
Endoleaks	8 (18.2)	18 (28.6)	.218[a]
Type IA	5 (11.4)	2 (3.2)	.056
Type IB	2 (4.6)	10 (15.9)	—
Type III	1 (2.3)	1 (1.6)	—
Type I or III	6 (13.6)	12 (19.1)	.462[a]
Type II	4 (9.1)	11 (17.5)	.220[a]
Aneurysm rupture	2 (4.6)	2 (3.2)	.573
Limb occlusion	3 (6.8)	6 (9.5)	.829[a]
Sac growth	6 (13.6)	16 (25.4)	.163[a]
Δ Sac volume, %	−9.1 (−29.9 to 0.0)	−11.7 (−29.2 to 2.8)	.692[a]
Migration >5 mm	1 (2.3)	2 (3.2)	.790[a]
Proximal seal loss >2 mm	11 (25.0)	10 (16.1)	.242[a]
Secondary interventions	9 (20.5)	17 (27.0)	.516
Proximal neck-related secondary interventions	3 (4.6)	4 (6.3)	.803
Proximal stent/cuff	1	4	—
Open conversion	2	0	—

AAA, Abdominal aortic aneurysm.
Dichotomous data are presented as number (%). Continuous data are presented as median (interquartile range [IQR]).
[a]*P* values obtained from log-rank test unless marked.

Statistical analysis. Categorical variables are presented as number and percentage and compared using the Pearson χ^2 test. Continuous variables are presented as mean (±standard deviation) or median (interquartile range [IQR]) if non-normally distributed and compared using the Student *t*-test or the Mann-Whitney *U* test, respectively. Severe proximal neck angulation was assessed as a risk factor for the main outcomes using Kaplan-Meier methods and multivariable Cox hazards regression models. Equality among survival curves was assessed with the Mantel-Cox log-rank test. Multivariable regression was performed including variables unequally distributed among groups at a $P \leq .1$ level. Confidence intervals (CIs) of 95% were used, and statistical significance was considered if $P \leq .05$. All statistical analysis was performed using Statistical Package for the Social Sciences 21.0 (IBM Inc, Armonk, NY).

RESULTS

During the early postoperative period, one patient in the angulated neck group and two control group patients died and were excluded from the current analysis. The angulated neck patient had a background of kidney dysfunction and died in another health care facility of renal complications on postoperative day 45. In the control group, one patient with known cardiac failure and valve disease died in the immediate postoperative period after urgent cardiac surgery. The third patient with a history of respiratory insufficiency died on postoperative day 13 of respiratory complications.

Of the remaining 107 patients, postoperative CTA imaging was available for all but 1 control group patient. This was a patient with renal insufficiency who, to date, had an uneventful clinical and DUS-based follow-up. The study population was observed for up to 9.6 years (median, 7.4 years; IQR, 4.8-8.5 years). Table I presents clinical and anatomic baseline characteristics. Groups did not differ in demographic variables and comorbidities. Regarding anatomic characteristics, mean α was 51.4 ± 21.1 degrees and 17.9 ± 17.0 degrees for the angulated and nonangulated groups; the mean β was 80.8 ± 15.6 degrees and 35.4 ± 20.0 degrees, respectively. AAA diameter was larger in the angulated neck group (mean, 68.6 ± 14.2 mm) compared with the nonangulated group (mean, 58.8 ± 7.6 mm; $P < .001$).

EL1A. During follow-up, seven patients (6.5%) developed EL1A; five patients (11.4%) in the angulated neck group and two patients (3.2%) in the control group (Table II). At 7 years, freedom from EL1A was 86.1% (n = 14;

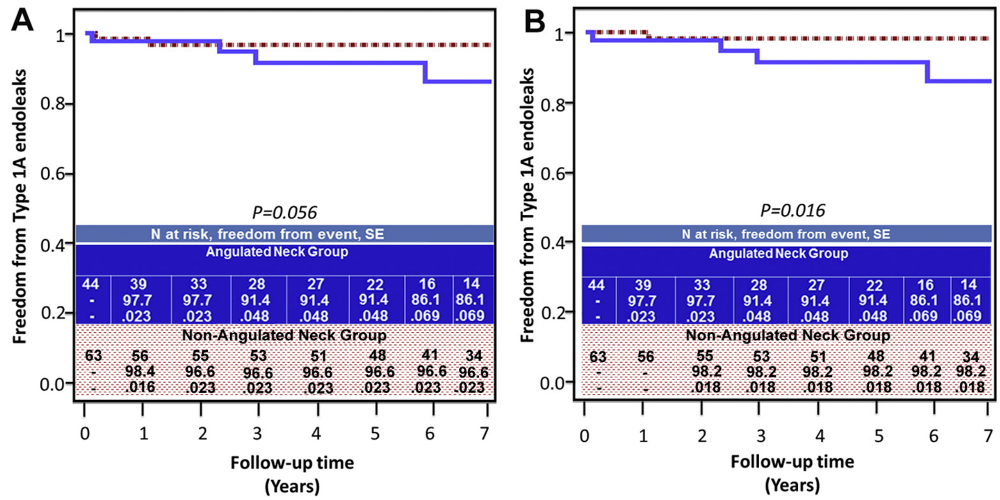

Fig 1. Freedom from type IA endoleak (EL1A). A divergence between the survival curves representing the angulated neck group (*continuous blue line*) and the control group (*dashed red line*) is observed (**A**; *P* = .056) and becomes statistically significant if the case of a patient with an endograft-related EL1A is excluded from the analysis (**B**; *P* = .016). *SE,* Standard error.

standard error [SE], 0.069) for the angulated neck group and 96.6% (n = 34; SE, 0.023) for the nonangulated group (*P* = .056; Fig 1, *A*). One patient from the control group presented with an endograft infection and secondary EL1A. Excluding this patient, this difference was significant, yielding a 7-year freedom from EL1A rate of 86.1% (n = 14; SE, 0.069) in the study group and 98.2% (n = 34; SE, 0.018) in the nonangulated group (*P* = .016; Fig 1, *B*). Although endograft oversizing was significantly different between groups (21.4% ± 10.2% in the angulated group, 16.1% ± 9.4% in the controls; *P* = .01), those angulated neck patients who developed EL1A had similar endograft oversizing compared with the remaining angulated group (mean oversizing was 20.4% ± 4.5% and 19.3% ± 12.5%, respectively; *P* = .54). In the angulated group, both α and β IFUs had been violated in 2 patients with EL1A (1 patient with a neck length 10-15 mm, α >45 degrees and β >60 degrees; 1 patient with a neck length >15 mm, α >60 degrees and β >75 degrees), whereas there were 12 other patients with both angulation IFUs breached who did not develop EL1A. Among the angulated neck group, there were no differences between patients who developed EL1A and the remaining group regarding baseline AAA diameter (median, 70.0 mm [IQR, 54.0-90.5 mm] vs 65.0 mm [IQR, 56.0-80.0 mm], respectively; *P* = .85), neck diameter (median, 25.0 mm [IQR, 21.5-32.0 mm] vs 25.0 mm [IQR, 22.0-28.0 mm]; *P* = .74), neck length (median, 28.0 mm [IQR, 18.0-36.5 mm] vs 28.0 mm [IQR, 15.0-35.0 mm]; *P* = 1.0), inverse-tapered neck configuration (1 [20%] vs 7 [18%]; *P* = .91), ≥50% circumferential involvement of the neck by thrombus (0 [0%] vs 3 [8%]; *P* = .52), or calcification (0 [0%] vs 8 [21%]; *P* = .26). Relevant morphologic and follow-up data of these patients developing EL1A are depicted in Table III.

Neck-related secondary interventions. Neck-related secondary interventions were performed in three patients in the angulated neck group and in four in the nonangulated group, yielding a 7-year freedom from neck-related secondary interventions of 91.7% (n = 14; SE, 0.059) and 91.6% (n = 29; SE, 0.029) in each group, respectively (*P* = .8; Table II). Of these, two angulated neck patients with EL1A underwent open conversion, whereas the other angulated neck patient had a fenestrated cuff implanted. Among those four control group patients, two had an EL1A, whereas two patients were treated pre-emptively because of impending loss of proximal seal. All four patients were treated with proximal cuffs (one fenestrated, three infrarenal cuffs).

Primary clinical success, aneurysm rupture, and mortality. At 7 years, primary clinical success was 41.2% (n = 11; SE, 0.085) in the angulated neck group and 56.6% (n = 20; SE, 0.072) in the nonangulated group (*P* = .12; Fig 2). In correcting for baseline differences (including preoperative AAA diameter, baseline aortic neck length, endograft oversizing, and proximal seal length at 30-day CT imaging), an increased risk of loss of primary clinical success was still not found for angulated neck patients (hazard ratio [HR], 1.16; 95% CI, 0.67-2.02; *P* = .59).

During follow-up, 25 patients died in the angulated neck group (56.8%) and 35 in the nonangulated group (55.6%). There were two ruptures in each group, which were fatal. Both angulated neck patients and one control group patient had AAA rupture due to EL1A. Overall survival at 7 years was 44.3% (n = 18; SE, 0.076) vs 66.7% (n = 42; SE, 0.059) for the angulated and control groups, respectively (*P* = .25; Fig 3). Seven-year freedom from

Table III. Patients developing type IA endoleak (*EL1A*): Clinical characteristics and consequences

Group	EL1A timing	PSL at 30-day CTA	Baseline hostile neck characteristics	EL1A diagnosis	Previous AAA-related events before EL1A	Findings on previous imaging	Interventions performed for EL1A	Outcome
Angulated	1 month	10 mm	α = 59 degrees β = 95degrees Diameter = 32 mm	Routine CTA	No	No intraoperative EL	No	Died of lower intestinal bleeding before undergoing EL1A treatment
Angulated	2 years	17 mm	α = 66 degrees β = 86 degrees	Intraoperative	Corrected type III EL 5 months before	4-mm endograft migration after limb relining, progressive sac growth, and PSL decrease	Open conversion	Uneventful recovery
Angulated	3 years	16 mm	α = 51 degrees β = 84 degrees	AAA rupture, CTA	Type IB EL detected 2 weeks before AAA rupture	Type IB EL, PSL decreased to 11 mm, no migration	No	Fatal AAA rupture; EL1A considered unamenable to endovascular repair, patient unfit for open repair
Angulated	6 years	15 mm	α = 43 degrees β = 91 degrees	AAA rupture, CTA	Transient type II EL at 30-day imaging only, undetectable subsequently	Previous CT performed 4 years before and subsequent DUS imaging unremarkable	Open conversion	Died in the immediate postoperative period
Angulated	8 years	25 mm	α = 26 degrees β = 76 degrees	Routine CTA	No	Progressive loss of PSL and AAA growth with 7-mm distal device migration	Proximal fenestrated cuff	Resolved EL1A
Control	2 months	14 mm	—	Endograft infection, CTA	Endograft infection	Type II EL on 30-day imaging, no signs of infection	Proximal infrarenal cuff, Palmaz stent	Patient unfit for open repair; AAA rupture and death
Control	2 years	33 mm	Diameter = 30 mm	Routine CTA	No	Type II EL on 30-day imaging	Proximal cuff, Palmaz stent, reballooning	Resolved EL1A

AAA, Abdominal aortic aneurysm; *CT*, computed tomography; *CTA*, computed tomography angiography; *DUS*, duplex ultrasound; *EL*, endoleak; *PSL*, proximal seal length.

aneurysm-related death was 92.3% (n = 18; SE, 0.54) vs 98.4% (n = 41; SE, 0.016) for the angulated neck and control groups, respectively (P = .28; Fig 3). In multivariable analysis correcting for baseline AAA diameter, infrarenal neck length, endograft oversizing, proximal seal length at 30-day CT imaging, and sex, patients with severe neck angulation did not have a risk of decreased overall survival (HR, 0.86; 95% CI, 0.4-1.7; P = .65).

Morphologic and device-related outcomes during follow-up. Median CT imaging follow-up was 3.0 years (IQR, 1.2-4.9 years) for the angulated neck group and 4.3 years (IQR, 2.1-6.2 years) for the nonangulated group (P = .09). At baseline, mean neck diameter was 25.2 mm and 25.5 mm for the angulated neck and nonangulated groups, respectively (P = .71; Table I). During follow-up, median neck dilation was 15.5% in the angulated neck group (IQR, 7.0%-27.2%) and 14.3% in the nonangulated group (IQR, 6.1%-23.2%; P = .66; Table IV). Proximal neck angulation changes were more pronounced in the angulated neck group at 30-day imaging but remained unchanged during subsequent follow-up (Table IV; Fig 4). Aneurysm sac growth occurred in 6 patients (13.6%) with severe neck angulation and in 16 control group patients (25.4%; P = .16).

At postoperative CT imaging, endograft migration >5 mm occurred in one angulated neck patient (2.3%) and in two patients in the nonangulated group (3.2%; P = .79). The angulated patient had begun with a proximal seal length of 17 mm and developed an EL1A 5 months after undergoing limb relining for a type III endoleak. An additional 4-mm distal displacement of the device was noted on routine imaging performed between the two events. The two patients in the control group both had inverse-tapered necks and >50% of circumferential thrombus. In both these cases, no clinical

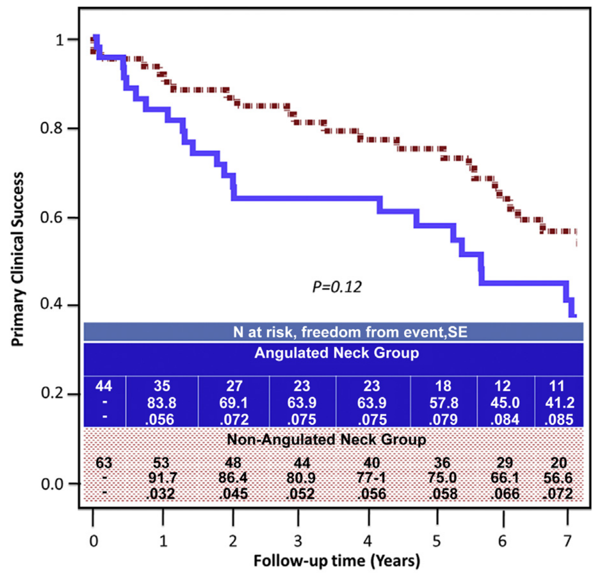

Fig 2. Primary clinical success. A divergence between the survival curves representing the angulated neck group (*continuous blue line*) and the control group (*dashed red line*) is observed soon after endovascular aneurysm repair (EVAR) but was not statistically significant ($P = .12$). *SE,* Standard error.

consequences were noted. Single barb detachments were encountered in 13 (12.2%) patients, 8 (18.2%) in the study group and 5 (7.9%) in the nonangulated group ($P = .12$), and all were first apparent on 30-day postoperative imaging. Multiple barb detachment or stent fracture was not identified.

DISCUSSION

To date, this study reports the longest term EVAR outcomes in patients with severely angulated necks. In this selected group of patients, despite the long proximal seal lengths obtained during initial implantation, an increased rate of EL1A was observed. In addition, angulated neck patients developing EL1A fared worse than the control group counterparts, requiring open conversion in most cases to correct the EL1A.

Proximal angulation decreases the necessary pull-down force required to dislodge the endograft.[16] In consequence, the expected increased risk of complications has excluded patients with severe neck angulation from all large trials, reducing the available evidence.[17,18] Some reports have challenged this concept.[19-21] In a study from AbuRahma et al,[20] neck angulation was not a risk factor for EL1A (odds ratio, 1.3; 95% CI, 0.5-3.1). Nevertheless, these favorable results may well have been due to the relatively short follow-up time (mean, 22 months). In contrast, several larger studies have associated proximal neck angulation with adverse outcomes after EVAR. In a report from Schanzer et al[3] (n = 10,228; mean follow-up, 31 months), β >60 degrees was an independent predictor of late sac expansion (HR, 2.0; 95% CI,

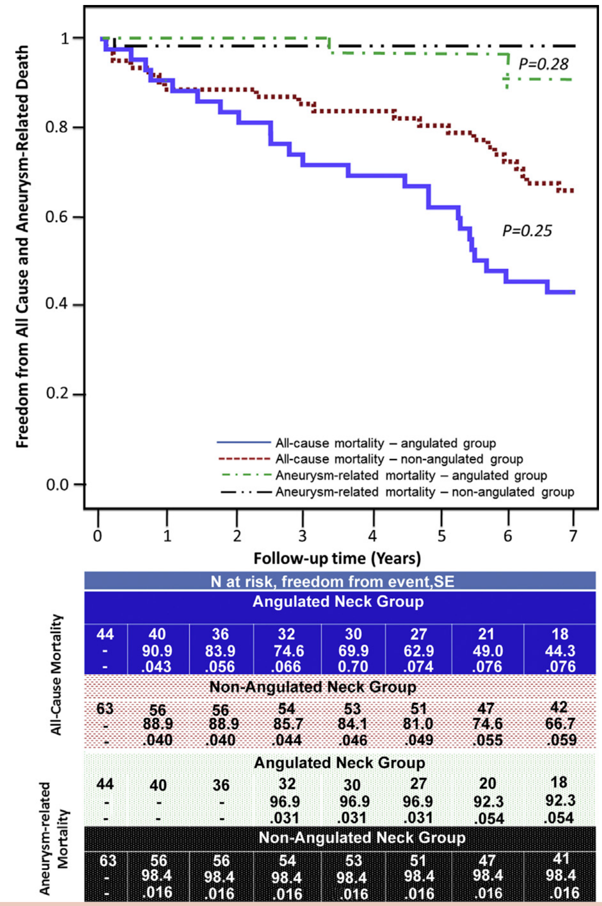

Fig 3. Freedom from all-cause and aneurysm-related mortality. No differences were observed in the survival curves for all-cause mortality (*continuous blue line*, angulated neck group; *dashed red line*, control group; $P = .25$) or aneurysm-related mortality (*dashed-dotted green line*, angulated-neck group; *dashed-dotted black line*, control group; $P = .28$). *SE,* Standard error.

1.6-2.4).[3] Tsilimparis et al,[22] reporting on 739 patients (all patients with 2-year follow-up, 158 with 5-year follow-up), also suggested that β angulation was a predictor of secondary interventions. In a report from Hobo et al[4] (n = 5183; mean follow-up, 19.9 months), β >60 degrees was associated with a higher risk of EL1A (HR, 1.8; 95% CI, 1.3-2.6). Noteworthy, most of these studies included several endografts, some of them even taken off the market many years ago. In addition, as each stent graft may have a different performance in challenging neck anatomy and the results were not stratified per device, these may be of limited applicability.

To overcome these limitations, design modifications have been introduced in a number of stent grafts, resulting in more conformable devices that adapt better to challenging anatomies and resist migration more, but longer term results on these late-generation endografts are scarce.[23] The 5-year results of the Aorfix endograft (Lombard Medical, Irvine, Calif) in the prospective multicentric Prospective Aneurysm Trial: High Angle Aorfix

Table IV. Morphologic evolution and device-related outcomes in the proximal neck

	Angulated (n = 44)	Nonangulated (n = 62)	*P* value
Neck dilation, %	15.5 (7.0-27.2)	14.3 (6.1-23.2)	.66
α Angle on 30-day imaging, degrees	36.6 (±18.3)	18.3 (±11.2)	<.001
β Angle on 30-day imaging, degrees	51.5 (±17.9)	25.6 (±12.7)	<.001
Δ α Angle at 30-day imaging, degrees	−14.5 (±19.1)	1.2 (±12.6)	<.001
Δ β Angle at 30-day imaging, degrees	−29.5 (±17.4)	−10.3 (±21.6)	<.001
Additional Δ α angle after 30-day imaging, degrees	1.2 (±14.3)	−1.8 (±12.0)	.47
Additional Δ β angle after 30-day imaging, degrees	−2.8 (±21.8)	9.9 (±17.2)	.003
Endograft migration distance, mm	1.0 (0.0-3.0)	0.0 (0.0-2.0)	.15
Single barb detachment	8 (18.2%)	5 (7.9%)	.12
Barb to inner aortic wall distance, mm	3.5 (1.5-5.9)	2.2 (1.6-2.9)	.62

Continuous data are presented as median (interquartile range [IQR]) or mean (±standard deviation).

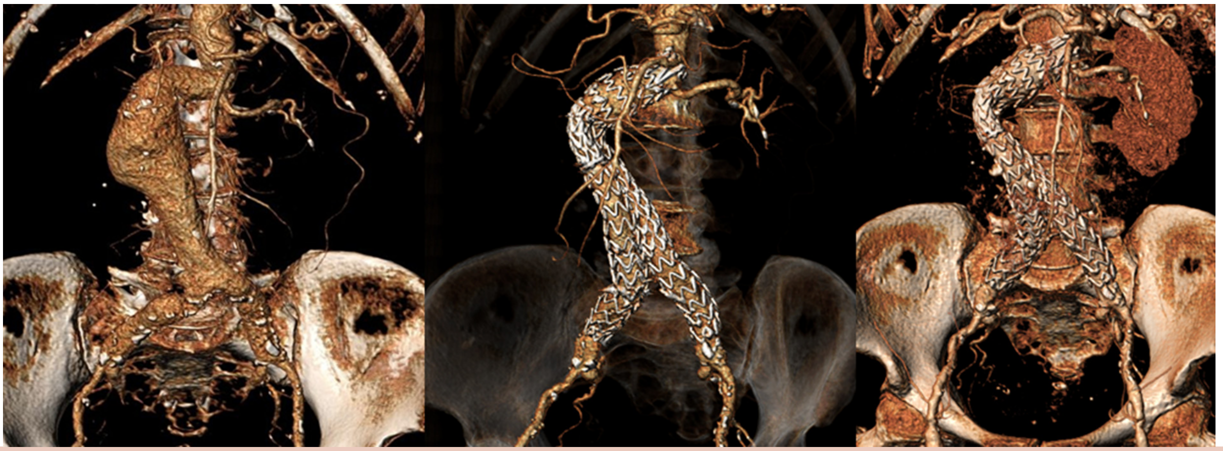

Fig 4. Evolution of proximal aneurysm neck angulation after endovascular aneurysm repair (EVAR) with the Endurant stent graft. *Left,* Baseline anatomy. *Middle,* One-year follow-up. *Right,* Four-year follow-up. No changes have been observed in the infrarenal aortic neck or the endograft position and seal in this severely angulated infrarenal neck.

Bifurcated Stent Graft (PYTHAGORAS trial) have been reported.[24] In comparing the 151 patients with β ≥60 degrees (42 patients with β >90 degrees) with the 67 patients with β <60 degrees, neck angulation was not associated with an increased risk of type I or type III endoleaks or >10-mm device migration. However, EL1A and neck-related secondary interventions were not individually reported. In addition, the 23% rate of stent fractures in the fixation zone may presage future seal complications. The Anaconda stent graft (Vascutek, Inchinnan, Glasgow, United Kingdom) is another highly flexible endograft with a design potentially suitable for angulated anatomies.[25] In a group of 36 patients treated with this device (mean infrarenal angulation was 82 degrees) with 4-year follow-up, one migration (with EL1A) and seven occlusions (two of the entire endograft) were reported. These may have been related to angulated neck anatomy, although this was not assessed. The Excluder Conformable Endoprosthesis (W. L. Gore & Associates, Flagstaff, Ariz) is another device specifically designed to deal with highly angulated proximal neck anatomy, but the investigational device exemption trial has yet to begin (ClinicalTrials.gov Identifier NCT02489539). Finally, the Endurant stent graft has been described before to perform well in challenging anatomies up to midterm, particularly in patients with severe neck angulation. In a report based on the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE; n = 1263) including 44 patients with α >60 degrees (3.6%) and 62 patients (5.1%) with β >75 degrees, Bastos Gonçalves et al[26] did not find an increased rate of neck-related complications among either group (*P* = .18 and *P* = .39, respectively). However, only 38% of the included patients had reached 2-year follow-up.

In our current study, despite favorable results having been reported on the same cohort at midterm,[9] a clinically worrisome increased rate of EL1A was found among angulated neck patients in the long term. In addition, whereas both control group patients with EL1A were able to be treated by endovascular techniques, this was possible for only one of five angulated neck patients with EL1A, leaving the remaining patients either to undergo open conversion or, if unfit, to face a high risk of AAA rupture. Importantly, the reported excessive rate of EL1A became significant when the one patient who developed an endograft infection and consequent loss of proximal seal months after implantation was excluded. This patient was expected to sustain clinical success if endograft infection had not developed, as his anatomy was within IFU. In assessing broader end points, such as primary clinical success, this difference was no longer apparent. Nevertheless, we emphasize that this study is limited by the sample size, which may explain the presented mixed results. Furthermore, this also hampered the possibility of correcting for other anatomic and device-related features in our analyses, such as AAA diameter, which was significantly larger among the angulated neck patients and may be associated with an increased risk of complications.[27] For this reason, we could not further specify which patients with severely angulated necks are at highest risk for development of complications. In our study, only rarely was severe neck angulation combined with other known hostile neck features. It is likely that the combination of several hostile features may greatly increase the risk of adverse events, as recently reported by Jordan et al.[28] In addition, the operators in the three centers were highly experienced in EVAR, which may potentially hamper the generalizability of the described results. For example, this may be particularly reflected during EVAR planning, in which deliberately greater oversizing (20%-30%) was used to accommodate the elliptical shape of the severely angulated infrarenal neck and any potential nonparallel device deployment in reference to the aortic walls, which is more likely to occur in angulated anatomy.[29,30] Additional procedural details in these patients included retraction of the stiff guidewires from the suprarenal aorta just before deployment and endograft deployment without any pull-back force, thus reducing straightening of the neck and promoting a better alignment of the stent graft to the patient's true anatomy. In case of difficulties in advancing the endograft into the proximal neck, a through-and-through stiff wire from the arm may provide additional support. However, in our opinion, while straightening the neck, additional tension is delivered to the neck and to the endograft's main body during deployment, which may result in endograft dislocation or migration after complete stiff wire removal. In our opinion, the endograft should adapt to the neck, and the other way around. In the event of using a through-and-through wire, we recommend "loosening" the wire during deployment. Still, only seldom was this technique used at the three participating centers. Finally, the selection of cases deemed "suitable" is an inherent bias that cannot be overcome. In high-risk patients with multiple hostile neck features, alternative endovascular options like parallel endograft techniques (chimney) may be considered. However, these may be technically challenging to perform, and long-term outcomes are lacking, especially in severely angulated necks. Adjunctive fixation with endoanchors during primary repair has been reported in patients with severe neck angulation to reduce lack of endograft apposition to the outer aortic curve, thus increasing proximal seal length.[27] However, reports are still scarce, and long-term durability is not known. For patients with reasonable surgical risk, open repair may still be the best solution as a long, severely angulated infrarenal neck is usually not a complicating factor for open repair.

Additional limitations of this study include its retrospective design and the lack of power calculation to determine the required sample size, according to expected event rates. These not only may have introduced a reporting bias but also are accountable for the different follow-up time between groups. However, patients were treated consecutively with the same endograft in the same hospitals during the same time period and observed prospectively. Although neck curvature may be a more accurate predictor of the aortic three-dimensional trajectory than angulation, this method is not available in most imaging reconstruction software and requires further investigation to determine its ability to predict long-term complications.[31] Also, at the time of this analysis, more than half of the original population has already died, and most of the surviving patients are followed up by DUS, which limits anatomic and device-related data collection. For these reasons, longer term reports on this specific cohort of patients will not be possible, and it is unlikely that a significantly larger study on this subject with similar long-term follow-up will be reported by others in the near future.

CONCLUSIONS

Despite initially long proximal seal lengths and satisfactory results in the early period, we identified an increased rate of EL1A during long-term follow-up among patients with severely angulated proximal neck anatomy. However, mortality was not affected by this difference. These findings suggest that EVAR should be used judiciously in patients with extreme angulation of the proximal neck and highlight the need for close follow-up of EVAR, especially in the long term and in patients treated outside IFU.

The authors would like to acknowledge the contributions of the following: Quirina M. B. de Ruiter, Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands, for technical assistance and demographic data collection; Debbie Werson, Department of Vascular Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands, for technical assistance and demographic data collection; and Richte Schuurmann, Department of Vascular Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands, for technical assistance during data collection.

AUTHOR CONTRIBUTIONS

Conception and design: NO, FG, HV
Analysis and interpretation: NO, SH, SR, JH, JV, HV
Data collection: NO, MR, KU, JP
Writing the article: NO
Critical revision of the article: NO, FG, SH, MR, KU, JP, SR, JH, JV, HV
Final approval of the article: NO, FG, SH, MR, KU, JP, SR, JH, JV, HV
Statistical analysis: NO, SH
Obtained funding: Not applicable
Overall responsibility: HV

REFERENCES

1. Dua A, Kuy S, Lee CJ, Upchurch GR Jr, Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. J Vasc Surg 2014;59:1512-7.
2. Chaikof EL, Fillinger MF, Matsumura JS, Rutherford RB, White GH, Blankensteijn JD, et al. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1061-6.
3. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation 2011;123:2848-55.
4. Hobo R, Kievit J, Leurs LJ, Buth J; EUROSTAR Collaborators. Influence of severe infrarenal aortic neck angulation on complications at the proximal neck following endovascular AAA repair: a EUROSTAR study. J Endovasc Ther 2007;14:1-11.
5. van Keulen JW, de Vries JP, Dekker H, Goncalves FB, Moll FL, Verhagen HJ, et al. One-year multicenter results of 100 abdominal aortic aneurysm patients treated with the Endurant stent graft. J Vasc Surg 2011;54:609-15.
6. Matsagkas M, Kouvelos G, Peroulis M, Avgos S, Arnaoutoglou E, Papa N, et al. Standard endovascular treatment of abdominal aortic aneurysms in patients with very short proximal necks using the Endurant stent graft. J Vasc Surg 2015;61:9-15.
7. Verhagen HJ, Torsello G, De Vries JP, Cuypers PH, Van Herwaarden JA, Florek HJ, et al. Endurant stent-graft system: preliminary report on an innovative treatment for challenging abdominal aortic aneurysm. J Cardiovasc Surg 2009;50:153-8.
8. Bastos Gonçalves F, de Vries JP, van Keulen JW, Dekker H, Moll FL, van Herwaarden JA, et al. Severe proximal aneurysm neck angulation: early results using the Endurant stentgraft system. Eur J Vasc Endovasc Surg 2011;41:193-200.
9. Oliveira NF, Bastos Gonçalves FM, de Vries JP, Ultee KH, Werson DA, Hoeks SE, et al. Mid-term results of EVAR in severe proximal aneurysm neck angulation. Eur J Vasc Endovasc Surg 2015;49:19-27.
10. Rouwet EV, Torsello G, de Vries JP, Cuypers P, van Herwaarden JA, Eckstein HH, et al. Final results of the prospective European trial of the Endurant stent graft for endovascular abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 2011;42:489-97.
11. Bastos Gonçalves F, van de Luijtgaarden KM, Hoeks SE, Hendriks JM, ten Raa S, Rouwet EV, et al. Adequate seal and no endoleak on the first postoperative computed tomography angiography as criteria for no additional imaging up to 5 years after endovascular aneurysm repair. J Vasc Surg 2013;57:1503-11.
12. van Prehn J, van der Wal MB, Vincken K, Bartels LW, Moll FL, van Herwaarden JA. Intra- and interobserver variability of aortic aneurysm volume measurement with fast CTA postprocessing software. J Endovasc Ther 2008;15:504-10.
13. van Keulen JW, Moll FL, Tolenaar JL, Verhagen HJ, van Herwaarden JA. Validation of a new standardized method to measure proximal aneurysm neck angulation. J Vasc Surg 2010;51:821-8.
14. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1048-60.
15. Balm R, Stokking R, Kaatee R, Blankensteijn JD, Eikelboom BC, van Leeuwen MS. Computed tomographic angiographic imaging of abdominal aortic aneurysms: implications for transfemoral endovascular aneurysm management. J Vasc Surg 1997;26:231-7.
16. Rahmani S, Grewal IS, Nabovati A, Doyle MG, Roche-Nagle G, Tse LW. Increasing angulation decreases measured aortic stent graft pullout forces. J Vasc Surg 2016;63:493-9.
17. Antoniou GA, Georgiadis GS, Antoniou SA, Kuhan G, Murray D. A meta-analysis of outcomes of endovascular abdominal aortic aneurysm repair in patients with hostile and friendly neck anatomy. J Vasc Surg 2013;57:527-38.
18. Sternbergh WC 3rd, Carter G, York JW, Yoselevitz M, Money SR. Aortic neck angulation predicts adverse outcome with endovascular abdominal aortic aneurysm repair. J Vasc Surg 2002;35:482-6.
19. Stather PW, Sayers RD, Cheah A, Wild JB, Bown MJ, Choke E. Outcomes of endovascular aneurysm repair in patients with hostile neck anatomy. Eur J Vasc Endovasc Surg 2012;44:556-61.
20. AbuRahma AF, Campbell JE, Mousa AY, Hass SM, Stone PA, Jain A, et al. Clinical outcomes for hostile versus favorable aortic neck anatomy in endovascular aortic aneurysm repair using modular devices. J Vasc Surg 2011;54:13-21.
21. Lal BK, Zhou W, Li Z, Kyriakides T, Matsumura J, Lederle FA, et al. Predictors and outcomes of endoleaks in the Veterans Affairs Open Versus Endovascular Repair (OVER) trial of abdominal aortic aneurysms. J Vasc Surg 2015;62:1394-404.
22. Tsilimparis N, Dayama A, Ricotta JJ 2nd. Remodeling of aortic aneurysm and aortic neck on follow-up after endovascular repair with suprarenal fixation. J Vasc Surg 2015;61:28-34.
23. Resch T, Malina M, Lindblad B, Malina J, Brunkwall J, Ivancev K. The impact of stent design on proximal stent-graft fixation in the abdominal aorta: an experimental study. Eur J Vasc Endovasc Surg 2000;20:190-5.
24. Malas MB, Hicks CW, Jordan WD Jr, Hodgson KJ, Mills JL Sr, Makaroun MS, et al. Five-year outcomes of the PYTHAGORAS U.S. clinical trial of the Aorfix endograft for endovascular aneurysm repair in patients with highly angulated aortic necks. J Vasc Surg 2017;65:1598-607.
25. Rodel SG, Zeebregts CJ, Huisman AB, Geelkerken RH; Multicenter Angulated Neck Study with the Anaconda study participants. Results of the Anaconda endovascular graft in abdominal aortic aneurysm with a severe angulated infrarenal neck. J Vasc Surg 2014;59:1495-1501, 1501.e1.

26. Bastos Gonçalves F, Hoeks SE, Teijink JA, Moll FL, Castro JA, Stolker RJ, et al. Risk factors for proximal neck complications after endovascular aneurysm repair using the Endurant stentgraft. Eur J Vasc Endovasc Surg 2015;49:156-62.
27. Schlosser FJ, de Vries JP, Chaudhuri A. Is it time to insert endoanchors into routine EVAR? Eur J Vasc Endovasc Surg 2017;53:458-9.
28. Jordan WD Jr, Ouriel K, Mehta M, Varnagy D, Moore WM Jr, Arko FR, et al. Outcome-based anatomic criteria for defining the hostile aortic neck. J Vasc Surg 2015;61:1383-90.e1.
29. Figueroa CA, Taylor CA, Yeh V, Chiou AJ, Zarins CK. Effect of curvature on displacement forces acting on aortic endografts: a 3-dimensional computational analysis. J Endovasc Ther 2009;16:284-94.
30. van Keulen JW, Moll FL, van Herwaarden JA. Tips and techniques for optimal stent graft placement in angulated aneurysm necks. J Vasc Surg 2010;52:1081-6.
31. Schuurmann RC, Ouriel K, Muhs BE, Jordan WD Jr, Ouriel RL, Boersen JT, et al. Aortic curvature as a predictor of intraoperative type Ia endoleak. J Vasc Surg 2016;63:596-602.

Submitted Dec 14, 2017; accepted Mar 26, 2018.